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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/869,159	08/15/2001	Tania Kastelic	1556.0290000	9266

7590 06/03/2004

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EXAMINER

QIAN, CELINE X

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 06/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/869,159

Applicant(s)

KASTELIC ET AL.

Examiner

Celine X Qian

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 March 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-9 and 15-17 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-9 and 15-17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 25 June 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date. _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1, 3-9, 15-17 are pending in the application.

This Office Action is in response to the Amendment filed on 3/18/04.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/18/04 has been entered.

Response to Amendment

The rejection of claims 4-7, 16 and 17 under 35 U.S.C. 102 (b) has been withdrawn in light of Applicant's amendment of the claims.

The rejection of claims 1, 3, 8, 9 and 15 under 35 U.S.C. 103 (a) has been withdrawn in light of Applicant's amendment of the claims.

Claims 4, 6, 16 and 17 are rejected under 35 U.S.C. 102 (b) for reasons discussed below.

Claims 1, 3, 5, 7-9 and 15 are rejected under 35 U.S.C. 103 (a) for reasons discussed below.

New Grounds of Rejection Necessitated by Applicant's Amendment

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 4, 6, 16 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Zubiaga et al. (1995, MCB, Vol 15, No.4, pages 2219-2230, see IDS).

The claims are drawn to a reporter gene DNA expression system comprising an expression cassette consisting of one or more genes encoding a protein having a detectable signal and 5' and 3' UTR sequences comprising operably-linked expression control elements; and 2) an instability region consisting of at least 20-100 nucleotides of the 3'UTR of a gene sequence which confers instability to a mRNA, and wherein the instability region is heterologous to the 3' UTR sequence. The claims are further drawn to an assay system comprising said expression system and a control expression system which does not have the mRNA instability sequence. The claims are also drawn to said expression system, wherein the instability region is from genes coding for cytokines, chemokines, GM-CSF, *c-fos*, etc.

Zubiaga et al. disclose an expression vector comprising *c-fos* promoter operatively linked to globin gene, wherein an ARE isolated from *c-fos* is inserted into 3'UTR of the globin gene (see page 2220, 2nd col., 6th paragraph). Zubiaga et al. also disclose that a control plasmid pRSV-lacZ, comprising a gene coding for expression of lacZ, 5' and 3'UTR for expression of said gene without mRNA instability sequence (see page 2221, 1st col., 2nd paragraph, lines 4-9). Zubiaga et al. further disclose that these construct are co-transfected into NIH-3T3 cells (see page 2221, 1st col., 2nd paragraph, lines 1-4). Therefore, Zubiaga et al. disclose the instantly claimed inventions.

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Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 3 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Banhozler et al., Zubiaga et al., in view of Zhang et al.

The claims are drawn to a method of screening for compounds which affect mRNA stability by using an expression system comprising reporter gene and a mRNA instability sequence inserted into 3'UTR of said reporter gene, contacting the system with one or more test compound, measuring the signal of the reporter construct.

The teaching of Banhozler is discussed in detail in the office action mailed on 6/17/03. However, Banhozler do not teach an expression system comprising a reporter gene, wherein the detectable signal of the encoded protein is measured for determining whether the compounds affect mRNA stability. Banholz et al. do not teach the mRNA stability sequence is heterologous to the 3' UTR of the reporter gene.

The teaching of Zhang is discussed in detail in the office action mailed on 6/17/03.

The teaching of Zubiaga is discussed above.

It would have been obvious to one of ordinary skill in the art to develop a method of screening compound that induce mRNA instability by using an expression cassette comprising a GFP reporter gene and a mRNA instability sequence inserted into 3'UTR of said reporter gene based on the teaching of Banhozler et al., Zubiaga et al., and Zhang et al. Banhozler et al. has

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demonstrated that compounds such as rapamycin can be tested for its ability to affect mRNA instability in a construct comprising the mRNA sequence down stream of the AP gene. Since the ARE instability region has already been identified as taught in Zubiaga et al., it can be inserted to 3'UTR of any known gene, including a reporter gene such as GFP. One of ordinary skill in the art would have been motivated to do so because the advantages offered by a GFP reporter over measuring mRNA stability by Northern blot, such as the non-invasive nature of direct measurement of fluorescent intensity. The level of skill in the art of molecular cloning is high. Absent evidence from the contrary, one of ordinary skill in the art would have reasonable expectation of success to make an expression cassette comprising a GFP reporter and mRNA instability sequence to screen for compounds that induce mRNA instability. Therefore, the invention would have been *prima facie* obvious to one of ordinary skill of art at the time the invention was made.

Claims 5, 7-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zubiaga et al., in view of Maniatis et al.

The claims are drawn to an assay system comprising a cell line stably transfected with a reporter gene DNA expression system comprising an expression cassette consisting of one or more genes encoding a protein having a detectable signal and 5' and 3' UTR sequences comprising operably-linked expression control elements; and 2) an instability region consisting of at least 20-100 nucleotides of the 3'UTR of a gene sequence which confers instability to a mRNA, and wherein the instability region is heterologous to the 3' UTR sequence, and a control system with mRNA instability sequence.

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The teaching of Zubiaga et al. is discussed above. However, Zubiaga et al. do not teach that the constructs are stably transfected in to a cell line.

Maniatis et al. teach a method of stably transfecting mammalian cells.

It would have been obvious to one of ordinary skill in the art to stably transfect the cell line with two expression systems as taught by Zubiaga et al. The ordinary artisan would have been motivated to do so for the ease of use of said cell line so that one does not have to transfect the cell line every time a compound needs to be tested. Using stably transfected cell line or transient transfected cell line for an assay is interchangeable and routine experimentation in the relevant art. The ordinary artisan would have reasonable expectation of success because of the teaching of Zubiaga et al., who teach an assay system comprising a cell line transfected reporter construct and control construct can be used to measure mRNA stability, and the teaching of Maniatis et al., who teach a method to stably transfect mammalian cells. Therefore, the invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

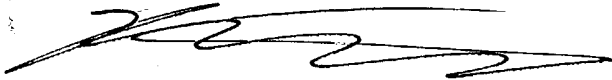
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Celine Qian, Ph.D.

A handwritten signature in black ink, appearing to be 'Celine Qian', written in a cursive style.